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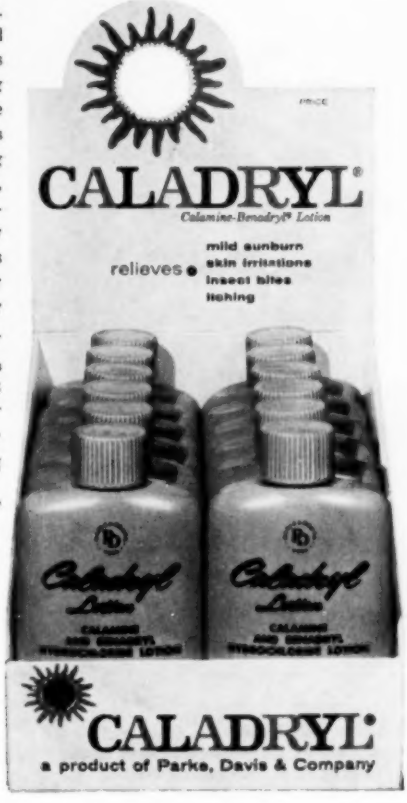

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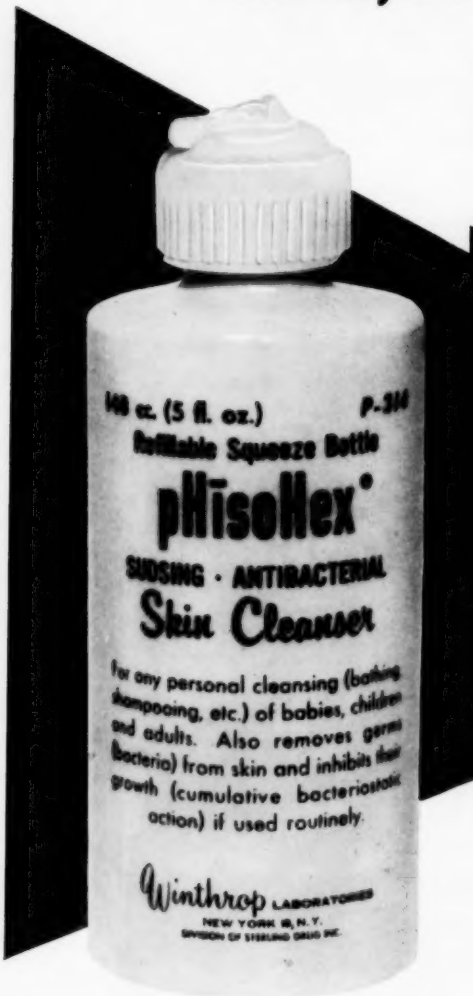


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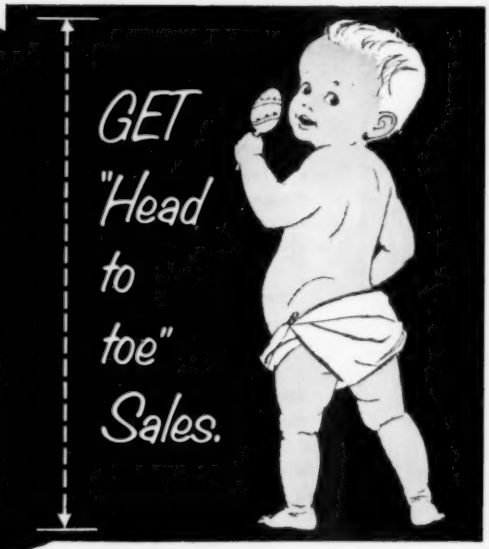


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# E D I T O R I A L

## OPPORTUNITIES UNLIMITED

AN amazing prediction has been made by experts studying the future of the ethical drug business in the United States. It is said that, in the next twenty years, the sales of prescription drugs will equal the present *total* drugstore sales including all sundries and sidelines. In reaching this conclusion, certain assumptions are made which seem entirely reasonable and, indeed, there is considerable evidence to substantiate this prediction. Two factors are of major importance in contributing to this tremendous growth in the use and sale of medicinals. One is the unprecedented growth in population which is predicted not only for the United States but for most countries in the world. The second is an increased standard of living for all persons, which will make them both willing and able to utilize the very best medical treatment available. Such a growth in prescription business is not so farfetched when one considers the fact that we have been experiencing just such a change in the last two decades. In fact, if the rate of growth continues as at present, there is not the slightest doubt as to this tremendous increase.

Another prediction which has been made, this time by those in pharmaceutical education, is that the number of practicing pharmacists in the United States is not likely to increase greatly in the next two decades. There are a number of reasons for this. First among these is the fact that pharmacy faces increasing competition by other fields, all needing highly capable young people as recruits. Some of the same abilities and skills required in pharmacy are also required in such fields as chemistry, engineering, physics, and electronics. These fields are very inviting to young people and strong bids are being made to gain their attention. The increased educational program in pharmacy, while it is essential, will serve to screen out of pharmacy's ranks all but the well-motivated and most capable applicants so that we are fairly certain not to have huge numbers of people entering the profession which, in times past, has done the profession great harm.

Now we come to the main theme of our editorial, "opportunities unlimited". If we can accept the two assumptions as outlined; namely, that the ethical drug business is to grow to an amazing degree and in twenty years equal the present total drugstore business and, if we furthermore accept the postulation that the over-all number of pharmacists will not increase greatly, then there is presented a golden opportunity for pharmacists to get back into professional activity. It is a well-known fact that the prescription department is the most profitable part of any pharmacy's operation. With the sales of such products mounting constantly, it would seem an entirely reasonable thing for pharmacists to gradually relinquish sidelines which show little profit at best and devote their time and attention to that area of their operation in which they have a monopoly justified by their professional training and competence. To take full advantage of this golden opportunity which the next two decades will present, it is more imperative than ever that pharmacists continue to justify their position as the sole distributors of prescription products. They must indeed be the experts in this field to which they lay claim, for this and only this can maintain their position.

Never in the history of our profession has there been a greater opportunity for us to grow in stature and prestige than now. This opportunity must be taken and there is reason for optimism that it shall be. Our profession may well be destined to enter a truly golden era.

L. F. Tice

# THE EFFECT OF RANCID OILS ON ANTIBIOTIC CONTAINING EMULSIONS [1, 2]

By Vasant G. Kudalkar,* Nathan A. Hall, and L. Wait Rising

PREVIOUS studies on the release of anti-infective substances from emulsion bases (1-3) have shown that the nature of the emulsion components may effect changes in the release of medication to such a degree that this factor must be considered in formulation studies. Since oils are often major constituents of emulsion systems, factors which affect their chemical composition need investigation. Rancidity, either oxidative or microbiological, has been shown to change the chemical nature of oils resulting in deterioration of odor and flavor. This study was designed to show the gross effect of this change upon the activity of antibiotic containing emulsions prepared from oils at varying stages of rancidity induced under controlled conditions.

## Experimental

A representative group of oils [3] of vegetable, animal, and mineral origin were selected, including peanut, castor, coconut, olive, corn,

* Present address: University of Bombay, Dept. of Chemical Technology, Bombay 19, India.

[1] Based on a thesis submitted to the Graduate School, University of Washington, by V. G. Kudalkar.

[2] Presented to the Scientific Section, A.Ph.A., Los Angeles Meeting, April, 1958.

[3] The authors wish to thank the following suppliers for generous supplies of substances used in this work:

| | |
|---|---|
| Peanut, Corn, Coconut Oils | E. F. Drew & Co., Inc. |
| Linseed Oil | Archer-Daniels-Midland & Co. |
| Castor Oil | E. R. Squibb & Sons |
| Codliver Oil | McKesson & Robbins, Inc. |
| Liquid Petrolatum | Standard Oil Co., of California |
| Penicillin G | Abbott Laboratories |
| Neomycin Sulfate | Eli Lilly and Co. |
| Bacitracin | Commercial Solvent Corp. |

linseed, codliver, and liquid petrolatum. The oils were subjected to controlled autoxidation by the method of King *et al.* (4) as modified by Riemenschneider (5) which involved the passage of purified air through the oil at 97.5° ± 1° C. for varying periods up to 100 hours. Since liquid petrolatum was oxidized too slowly by the method, the procedure was applied while the sample was exposed to ultraviolet light from a mercury vapor lamp. As a control measure, the peroxide value by the method of Wath and Major (6) and the acid value by the U. S. P. method (7) were determined for each sample. Each oil sample was also evaluated by its odor. Early stages of oxidation were best indicated by the peroxide value and later stages, by the acid value.

Oils which had been subjected to controlled oxidation for 0, 10, 20, 30, 40, 50, and 60 hours were incorporated into the following simple oil-in-water emulsion formula:

| | |
|---|---|
| Oil | 50 parts |
| Sorenson Phosphate Buffer [4] | 50 parts |
| Emulsifying Agent [5] | 2 parts |

To separate samples of each emulsion were added potassium penicillin G [6] (2.5, 5, and 10 units per ml.) neomycin sulfate [6] (5, 10, 20 micrograms per ml.) and bacitracin [6] (10, 20, 40 and 80, 160, 320 units per ml.) to furnish three concentration ranges for each antibiotic. The emulsions were then assayed for antibiotic activity by the F. D. A. Cup-plate method (8). Penicillin and neomycin assays were performed with *Staphylococcus aureus* ATCC #6538P as a test organism and bacitracin assays were performed both with *Staphylococcus aureus* and with *Micrococcus flavus* (bacitracin strain) ATCC #10240. Both Tween 60 and Tween 61 were found to be inhibitory to *Micrococcus flavus;* therefore, bacitracin activity was determined against *Staphylococcus aureus* also. Four plates were used for each emulsion: one for each of the three antibiotic concentrations and one for an emulsion blank containing no antibiotic. Inhibitory activity was measured by determining the average diameter of zones of inhibition for 5 samples. Results were examined for significance by application of the "student

[4] pH 6.25 for penicillin and bacitracin emulsions. pH 8.04 for neomycin.

[5] Tween 61 for all emulsions except Tween 60 for codliver oil and liquid petrolatum emulsions. Liquid petrolatum required 4 parts of emulsifier.

[6] See footnote no. 3.

t-test" ($P = 0.01$) for emulsions containing each oil. The least significant differences varied from 0.6 to 0.7 mm. for the method.

In all instances, no significant differences between the activity of emulsions containing untreated oils and oils which had no detectable rancid odor were evident. However, differences were apparent when oils of higher degrees of rancidity were used. Activity differences were found to be correlatable with the high acid value of the oil. Castor oil and coconut oil, which were quite resistant to autoxidation, exerted no significant influence on the activity of any of the three antibiotics.

*Penicillin.*—Increasing rancidity of peanut, olive, corn, linseed, and codliver oil resulted in slightly more active emulsions than those prepared with non-rancid oil. A characteristic graph of the effect is shown in Figure 1. Increasing rancidity of liquid petrolatum resulted in a decrease of penicillin activity.

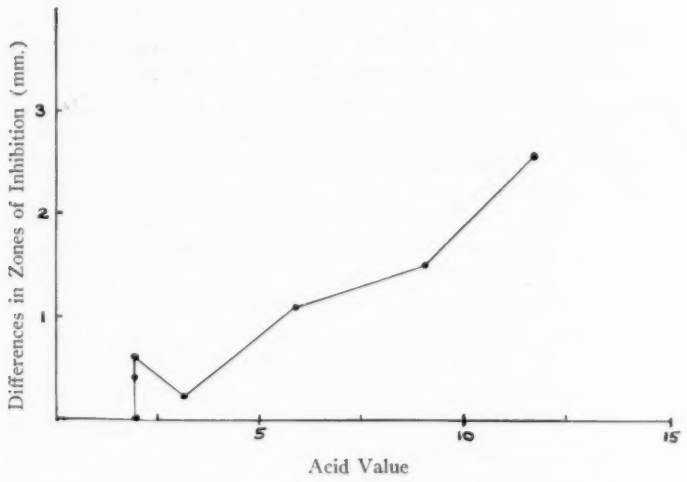


FIGURE 1. Effect of rancid olive oil on activity of emulsions containing penicillin (10 mcg. per ml.). Differences in zones of inhibition were determined by subtraction of the zones of inhibition of the non-rancid control emulsion from that of the rancid oil emulsion; thus, a positive difference indicates increased activity in the rancid oil emulsions.

*Bacitracin.*—Increasing rancidity of peanut, olive, corn oils, and liquid petrolatum resulted in a decrease of activity. Typical results are shown in Figure 2. No significant effect was observed with increasing rancidity of linseed or codliver oils even though their rancidity was marked.

*Neomycin.*—As the degree of rancidity increased in peanut, olive, corn, linseed, and codliver oil, the activity of emulsions decreased markedly and disappeared completely in the case of the most rancid samples. A typical result is shown graphically in Figure 3. The same effect was noticeable with liquid petrolatum emulsions at low antibiotic concentrations.

*The Inactivation of Neomycin Sulfate*

Several preliminary experiments were conducted to examine in more detail the nature of the inactivation of neomycin sulfate. Since

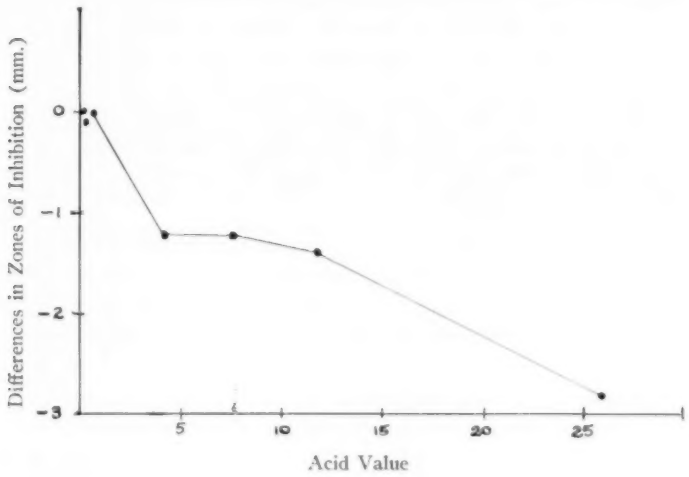


FIGURE 2. Effect of rancid peanut oil on activity of emulsions containing bacitracin (160 mcg. per ml.). Test organism—*Staphylococcus aureus.* Differences in zones of inhibition were determined by subtraction of the zone of inhibition of the non-rancid control emulsions from that of the rancid oil emulsion; thus, a negative difference indicates decreased activity for the rancid oil emulsions.

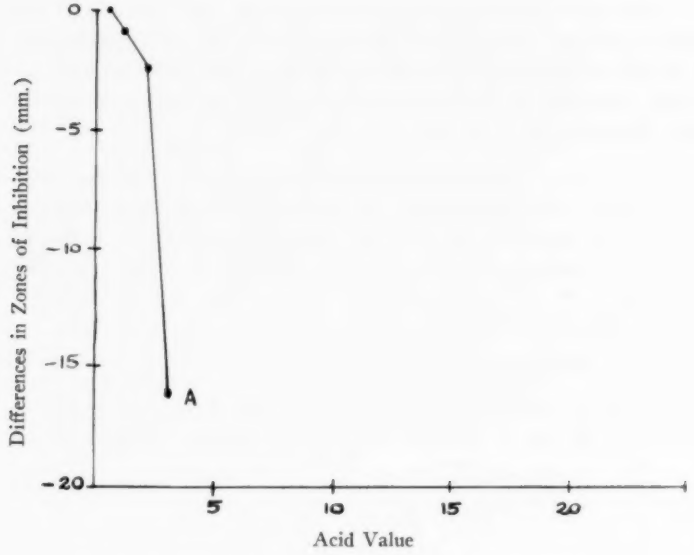


FIGURE 3. Effect of rancid corn oil on activity of emulsions containing neomycin sulfate (10 mcg. per ml.). Differences in zones of inhibition were determined by subtraction of the zone of inhibition of the non-rancid control emulsion from that of the rancid oil emulsion; thus, a negative difference indicates decreased activity for the rancid oil emulsions. Activity disappeared at Point A.

in some instances only partial inactivation of the emulsions occurred, an experiment was designed to show the effect of time on the inactivation. A highly rancid corn oil (acid value 7.1, peroxide value 537) was used for the emulsions and the results shown in Table I were obtained.

TABLE I

EFFECT OF STORAGE ON NEOMYCIN SULFATE INACTIVATION [a]

| | | *Period of Storage (Hours)* | | |
|---|---|---|---|---|
| *Rancid Corn Oil Emulsion* | *Control* | *0* | *48* | *96* |
| Neomycin Sulfate (0.5 mg./ml.) | 19.5 | 14.3 | 0 | 0 |
| Neomycin Sulfate (1.0 mg./ml.) | 20.0 | 16.7 | 12.4 | 0 |

[a] Values represent zones of inhibition in mm. and are the averages of at least 5 readings.

The results indicated that the reaction of inactivation was fairly slow.

The activity in all experiments was observed to disappear at pH 7-8. Therefore, a series of fresh corn oil emulsions containing neomycin were prepared buffered with phosphate buffers in a pH range of 6.95 to 7.95. Although a slight decrease in activity occurred with increasing acidity, no marked loss of activity was evident, indicating the hydrogen ion concentration alone was not responsible for the inactivation.

Rancid corn oil samples were treated with sufficient alcoholic KOH to neutralize the free acids in a peroxide-free ether solution. After removal of the solvents, the neutralized oils were used to prepare neomycin emulsions which were assayed for activity. No protection of neomycin activity was afforded by neutralization of the free acids.

Since the foregoing experiments indicated that the anion of the acidic component was involved in the inactivation, chromatographic separation of the acids of rancidity was attempted. An ether solution of rancid corn oil was passed through an alumina column according to the method of Sylvester *et al.* (9). The acids were strongly adsorbed allowing the remainder of the oil to be eluted from the column with ether. After removal of the ether, the oil was incorporated with neomycin-containing emulsions which were tested for activity. The results (Table II) revealed that the inactivating substances had been removed chromatographically and that a moderate peroxide content had little effect upon the activity of the emulsion.

TABLE II

THE RESULTS OF THE REMOVAL OF NEOMYCIN-INACTIVATING FACTORS FROM CORN OIL BY CHROMATOGRAPHY

| | | | *Neomycin Sulfate Concentration* | | | |
|---|---|---|---|---|---|---|
| | *Acid* | *Peroxide* | *5/ml.* | *10/ml.* | *20/ml.* | |
| *Nature of Oil* | *Value* | *Value* | *Zone of Inhibition (mm.)* | | | *pH* [a] |
| Non-rancid | 0.612 | 98.3 | 11.5 | 12.6 | 14.0 | 7.90 |
| Rancid [b] | 7.50 | 401 | 0.0 | 0.0 | 0.0 | 7.35 |
| Chromatographed Rancid | 0.719 | 260 | 11.5 | 12.8 | 14.1 | 7.90 |

[a] Determined with Beckman Model H-2 pH meter.

[b] Subjected to controlled autoxidation for 40 hours.

Several neomycin sulfate emulsions were prepared from peanut oil to which synthetic acids likely to be formed in rancidity were added. A sufficient quantity of n-caprylic and pelargonic acids was added to fresh oil samples to give acid values at which neomycin inactivation was observed to occur. Emulsions containing the fortified oils were then tested for activity which was compared with that obtained when control samples of non-rancid and rancid oils were used. Although some inactivation occurred with the acid-fortified fresh oil, in no instance was it comparable to that of the highly rancid oil.

An attempt was made to extract the active form of neomycin from the inactive emulsions. Highly rancid corn oil emulsions which originally contained 1 mg. per ml. of neomycin sulfate were extracted with peroxide-free ether to remove the oil and the resulting mixture was extracted with four successive 25 ml. portions of pH 8.04 phosphate buffer. The aqueous buffer extracts were again extracted with ether to remove the remaining traces of oil. As a control, fresh corn oil emulsions containing 1 mg. per ml. were subjected to the identical extraction procedure. Testing of aqueous extracts showed no detectable activity from the rancid oil emulsions and slightly reduced activity from the fresh oil emulsions. This experiment indicated that the neomycin had undergone some chemical transformation involving either decomposition or conversion to a water-insoluble form. Further studies of the inactivation are in progress.

## Discussion

Although it is obvious that rancid oils are undesirable for preparation of emulsions from an esthetic viewpoint, the foregoing experiments indicate that certain antibiotics contained in such emulsions may undergo changes which will noticeably influence their activity. The oils which are rancid enough to be organoleptically objectionable are most apt to cause changes; however, it might be postulated that with time even those oils which are organoleptically sound might exert some activity. Further studies of the effect of emulsions containing oils of low rancidity on storage are indicated.

The factors which are detrimental to the activity of neomycin sulfate appear to be associated with the acids formed on rancidification. Possibly they may be reacting with neomycin to form water-insoluble salts which show no activity in the predominantly aqueous agar cup-

plate test medium. Since the antibiotic is reported to have high stability (10), its chemical destruction would be unusual.

## Summary

Peanut oil, corn oil, olive oil, coconut oil, castor oil, linseed oil, codliver oil, and liquid petrolatum were subjected to controlled autoxidation at 97.5° for varying periods of time to produce different degrees of rancidity. The resulting oils were incorporated into simple emulsions containing potassium pencillin G, bacitracin, and neomycin sulfate and tested immediately for activity by the agar cup-plate method. Usually, the activity of penicillin was enhanced and the activity of bacitracin was inhibited by rancid oils. The activity of neomycin was destroyed completely by highly rancid oils. Preliminary examination of the destructive influence indicated that the acids formed on rancidification were involved.

Rancidification was followed by determination of the peroxide value, acid value, and organoleptically. The effect of the oils on antibiotic activity appeared to parallel the increase in acid value. Generally, no effect on activity was noted with oils of slight or moderate rancidity and, in all instances where antibiotic activity was affected, the oils had a definite rancid odor.

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# A SURVEY OF HOSPITAL PHARMACY AS VIEWED BY THE NURSING SERVICE

By Benjamin Teplitsky *

IN his ever expanding professional role, the hospital pharmacist works hand in hand with many services in the interest of the patient. One of these services with which the pharmacist has daily contact is the nursing service.

In order to determine the nature and degree of professional co-operation between the nursing and pharmacy services—as viewed by Chief Nurses—questionnaires were mailed to 131 Chief Nurses of the larger hospitals throughout the 49 states.

Replies were received from 111 hospitals—an 85% return—representing a total bed capacity of 164,070. These hospitals represent every state in the United States.

The unusually high and enthusiastic response in itself indicates the nursing services' keen interest regarding the pharmacy service in hospitals. The statistics compiled from this questionnaire are the basis of this article.

*Question 1: "Does the hospital pharmacist lecture to nurses?"*

Among the Chief Nurses 12% indicated that the pharmacist lectures to nurses *regularly*, 54% said that the pharmacist lectures only *occasionally*, while 34% stated that the pharmacist *never* lectures to the nurses.

*Comment:* The hospital pharmacist has a wonderful opportunity to promote hospital pharmacy by volunteering his services and lecturing to the nurses regularly. It is true that the work-load in many hospitals makes this a difficult task, especially in one-man pharmacies. Under such circumstances, the pharmacist is urged to select a convenient time when the work-load permits. By lecturing to nursing personnel, the pharmacist creates mutual trust and greater understanding of his service in the over-all picture of patient care. Current problems affecting each service are discussed and information shared. The pharmacist has a wealth of knowledge, both administrative and professional, at his command, and such knowledge serves

* Chief, Pharmacy Service, Veterans Administration Hospital, Albany, New York.

its useful purpose only when properly disseminated. The lectures should be a place for exchange of information and ideas. At the conclusion of any one session, each service should better understand each other's problems, and the end result is always better and improved patient care.

*Question 2: "If so, does he lecture on administrative procedures related to the Pharmacy?"*

Of the total hospitals checked, 61% said "Yes" and 39% said "No".

*Comment:* The non-professional aspects of the operation of hospital pharmacy—such as requisitioning procedures, drug charges, return of non-usable or accumulated drugs, pick-up and delivery procedures—are an integral part of hospital pharmacy and are important to the over-all operation. It, therefore, behooves the hospital pharmacist to be constantly on the alert to orient nursing personnel, especially new ones, and review with the regular nursing staff the rules and regulations pertaining to these administrative procedures governing the operation of the hospital pharmacy.

The hospital pharmacist must understand the problems confronting the nursing personnel and nursing personnel must understand pharmacy's problems. If the Nursing Service fails to use proper order procedures, orders excessive amounts, fails to check on deteriorated drug stocks on the ward, the hospital pharmacist should make it a point to correct such discrepancies during regular lectures to them. If the nursing personnel is displeased with some late drug deliveries from the pharmacy, lack of drug information dissemination to the nurses, deletion of certain drug requests, problems in drug nomenclature—all such problems should be brought up at such sessions for discussion and clarification. Mutual problems may thus be resolved.

*Question 3: "Does he lecture on new drugs and other professional subjects?"*

On this question 56% said "Yes" and 44% said "No."

*Comment:* For almost half of hospitals' pharmacists not to take advantage of their natural talent and qualifications to lecture to the professional staff appears almost criminal.

The hospital pharmacist should not wait to give an occasional lecture when requested to do so by the Nursing Service, but should volunteer his services at regular intervals. Once his services are "tasted", the pharmacist will have no trouble arranging for regular lectures to nurses, nursing students, interns or even residents. His up-to-date knowledge of drugs, dosages, contraindications, side-effects, and general knowledge of drug therapy makes him an expert in the field.

Lecturing to nurses and nursing students in hospitals with schools of nursing should be a must for hospital pharmacists. "The Hospital Pharmacist as an Instructor of Pharmacology in the Nursing Educational Program", an article appearing in the August 1958 issue of the AMERICAN JOURNAL OF HOSPITAL PHARMACY, written by Sister M. Gonzales and Gerard Wolf is excellent material for any pharmacist who has intentions of initiating or improving upon his own procedure.

The hospital pharmacist should stress new drugs as they are introduced into his hospital. The pharmacist should make available to nursing personnel visual aids, such as conversion charts, dosage charts, or even anatomical charts prepared by drug manufacturers for professional use. He should assist the nursing personnel in obtaining films also made available by drug manufacturers. All these aids should be used to supplement his professional lectures.

*Question 4: "Does the hospital pharmacist check ward drug cabinets regularly?"*

Of the total hospitals reporting, 57% said "Yes", and 43% said "No."

*Comment:* The proper care of ward drug cabinets directly reflects the supervision by the chief pharmacist of the hospital. A clean and orderly drug cabinet indicates good drug habits originating at the pharmacy and encompassing the nursing unit.

In making these inspections, the pharmacist should always be accompanied by a supervisor nurse. The pharmacist is then able to point out irregularities of drug maintenance and at the same time, have something complimentary to say to the supervisor when the drug cabinets are in proper order. The supervisor nurse can observe the inspection by the pharmacist and allow the duty nurse to perform

her regular work. The information received by the supervisor nurse is then relayed to the nurse in charge of the ward being inspected.

In the interest of patient safety and hospital economy, periodic inspections of drugs on wards become almost a necessity. Inspections per se are not enough. It is important that, following such inspections, deficiencies observed should be checked again to determine whether they have been corrected.

*Question 5: "Are nurses taken through the hospital pharmacy shortly after they are employed by the hospital?"*

It was interesting to observe that 55% said "Yes" and 45% said "No."

*Comment:* Meeting new nurses and taking 15 minutes of your time to describe your pharmacy operation may be a minor incident, but such "hospitality" makes a favorable impression on the nurses. At the same time, you have an opportunity to emphasize your desire to be of service to them. Many times, such meetings will erase erroneous impressions that nurses may bring from elsewhere.

*Question 6: "Is a literature file of current drugs maintained by the Nursing Department?"*

The high percentage of 73% saying "Yes" was a pleasant surprise. The 27% who said "No" still represent a substantial group who, with some assistance from the pharmacy, may be able to start one.

*Question 7: "Does the pharmacist provide literature for such files?"*

Of all the nursing departments maintaining literature files, 66% said that they do receive literature from the pharmacist while 34% said "No."

*Comment:* The hospital pharmacist has a close relationship with the medical service representatives of various drug manufacturers. Because he is in a good position not only to obtain literature from manufacturers, but to be selective in the type of literature the nurses desire, the hospital pharmacist should offer his services to the Director of Nursing in supplying current drug literature for their files.

*Question 8: "What number of days is the pharmacy open?"*

The survey revealed the following information:

| | |
|---|---|
| 7 days | 49% |
| 6½ days | 5% |
| 6 days | 10% |
| 5½ days | 21% |
| 5 days | 15% |

*Question 9: "Do nurses have occasion to dispense drugs from the pharmacy?"*

The replies to this question were most surprising. Over half of the hospitals—52%—answered "Yes", and 48% said "No."

*Comment:* Nurses should never be charged with the pharmacists' duties of dispensing, manufacturing, bottling, or labeling of medications—unless they are under the direct supervision of a pharmacist. Legally, the hospital pharmacist is generally the responsible person for all medications issued to patients from the hospital pharmacy. It, therefore, behooves him to see that no unauthorized personnel become involved in discharging a professional responsibility for which only the pharmacist is fully qualified.

*Question 10A: "Is there a full-time pharmacist at the hospital pharmacy?"*

Although the larger hospitals of each state were selected, the survey indicated that only 86% had a full-time pharmacist and 14% did not. This 14% represented 15 hospitals with a total bed capacity of 22,511. Mental hospitals constituted the bulk of those without a pharmacist.

*Comment:* Today, this is surprising because the advance of drug therapy in psychiatry certainly presents a greater need for pharmacy service in a mental hospital now than it did many years ago.

*Question 10B: "If not, is there a need for a full-time or part-time pharmacist?"*

(This question pertains to hospitals without a full-time pharmacist.)

Of the 15 hospitals not having a full-time pharmacist, ⅔ thought a part-time pharmacist would suffice and ⅓ said there is a need for a full-time pharmacist.

*Question 11: "Are narcotics delivered to wards or picked up by nurses or both picked up and delivered?"*

The hospitals reported as follows:

| | |
|---|---|
| a) Delivered to wards | 19% |
| b) Picked up by nurses from pharmacy | 68% |
| c) Both delivered on occasion and picked up | 13% |

*Comment:* Some hospitals indicated that the nurse from the operating room picked up narcotics for the entire nursing department; some indicated that the pharmacist delivered all narcotics to the supervisor's office for distribution to all nursing units; other hospitals indicated that only a registered nurse was authorized to pick up narcotics.

*Question 12: "Are routine drugs delivered by pharmacy personnel or picked up by nursing personnel?"*

Of the hospitals reporting, 33% indicated that routine drugs were delivered by pharmacy personnel and 67% said that nursing personnel picked up drugs from the pharmacy.

*Comment:* Numerous hospitals indicated that drugs were delivered to nursing units by means of elevators, dumb waiters, messenger services, and conveyor systems. The author finds that the use of pharmacy personnel (non-professional) is most satisfactory. The pick-up of empty drug baskets and delivery of drugs is then completely in the hands of the pharmacy. The entire procedure may then be accomplished with a minimum of lost time both for the nursing and pharmacy departments.

*Question 13: "Does a nurse regularly attend meetings of the Hospital Pharmacy Drug Committee?"*

Of the hospitals reporting, 17% said "Yes" and 83% said "No."

*Comment:* Although only 17% of the hospitals have nurses attend meetings of the Pharmacy-Drug Committee, it is hoped that a nurse will soon become a permanent member of such Committee.

## COMMENTS ON HOW PHARMACIST CAN BE MORE HELPFUL TO NURSES

As Submitted by Directors of Nursing Service

1. A nurse and a pharmacist should check ward stocks *together* periodically.
2. The pharmacist should obtain more literature for the Nursing Service.
3. One of the pharmacists should attend the Nurses Administrative Committee meetings regularly.
4. The pharmacist should assist in teaching of Drugs and Solutions.
5. Pharmacist should lecture to staff on new and current drug products.
6. The pharmacist should replenish daily the drugs used from the Emergency supply on all Nursing Units.
7. The Pharmacy should be covered by a pharmacist at all times.
8. The pharmacist should follow the requests as ordered—not send a lot more at times and less at other times.
9. Pharmacy personnel should check medication cupboard on each ward and keep them supplied; they should deliver drugs. Many nursing hours are wasted by nurses running errands for other departments.
10. There should exist close cooperation between the departments of Pharmacy and Nursing.
11. The pharmacist should standardize all labels on medication containers maintained by the Nursing Units.
12. The pharmacist should deliver narcotics.
13. The pharmacist should teach pharmacology to student nurses and also give in-service education talks.
14. The pharmacist should provide a system of delivering drugs to Nursing Units and pick up drug requests from the Nursing Units.

15. The pharmacist and nursing director should keep each other informed concerning changes in nursing procedure and pharmacy procedures that affect other units.

16. The pharmacist should teach elementary pharmacology to aides.

17. The pharmacist should keep nursing service abreast of latest developments in medicinal agents.

18. The pharmacist should be invited to nursing service meetings.

19. The pharmacist should supply the nursing service with up-to-date literature on new drugs and provide each ward with a *Physician's Desk Reference.*

20. The pharmacist should supply information on new drugs at the request of individual nurses.

21. The pharmacist should aid the nursing units in establishing literature files and assist the nurses in maintaining them.

22. Problems concerning pharmacy and nursing units should be resolved by means of conferences between the nursing director and the chief pharmacist.

23. The pharmacist should work for some uniformity of naming of drugs.


RESUMÉ

Questionnaires Sent — 131
Questionnaires Replied — 111
Bed Capacity of Returned Questionnaires—164,070

Question 1: "Does the Hospital Pharmacist lecture to nurses?"
Occasionally — 54%
Regularly — 12%
Never — 34%

Question 2: "If so, does he lecture on administrative procedures related to Pharmacy?"
Yes — 61%
No — 39%

Question 3: "Does he lecture on new drugs and other professional subjects?"

Yes — 56%
No — 44%

Question 4: "Does the hospital pharmacist check ward drug cabinets regularly?"

Yes — 57%
No — 43%

Question 5: "Are nurses taken through the hospital pharmacy shortly after they are employed by the hospital?"

Yes — 55%
No — 45%

Question 6: "Is a literature file of current drugs maintained by the Nursing Department?"

Yes — 73%
No — 27%

Question 7: "Does the pharmacist provide literature for such files?"

Yes — 66%
No — 34%

Question 8: "What number of days is the pharmacy open?"

5 days — 15%
5½ days — 21%
6 days — 10%
6½ days — 5%
7 days — 49%

Question 9: "Do nurses have occasion to dispense drugs from the pharmacy?"

Yes — 52%
No — 48%

Question 10-A: "Is there a full-time pharmacist at the hospital pharmacy?"

Yes — 86%
No — 14%

Question 10-B: "If not, is there a need for a full-time pharmacist at the hospital?"

Yes — 34%

Or for a part-time pharmacist?

Yes — 66%

Question 11: "Are Narcotics:

Delivered to ward? — 19%

Picked up by nurse from pharmacy? — 68%

Both delivered on occasion and picked up? — 13%

Question 12: "Are routine drugs:

Delivered by Pharmacy personnel? — 33%

Picked up by Nursing personnel? — 67%

Question 13: "Does a nurse regularly attend meetings of the Hospital Pharmacy Drug Committee?"

Yes — 17%

No — 83%

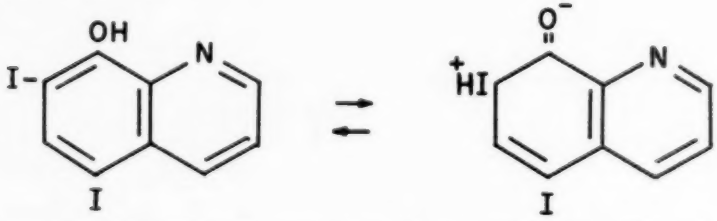
# ASSAY OF DIIODOHYDROXYQUIN BY NON-AQUEOUS TITRATION

By H. H. Kavarana *

*A method for the determination of diiodohydroxyquin by a nonaqueous titration method is described in detail. The method is simple and well suited for product control in the pharmaceutical industry. The method can also be applied to the assay of diiodohydroxyquin in tablets.*

THE compound diiodohydroxyquinoline (8-hydroxy-5,7-diiodoquinoline) is official in the U. S. P., the B. P., and several other pharmacopoeias. It is an accepted antiprotozoal agent, widely used because of its low toxicity in the treatment of amebic dysentery and intestinal amebiasis. The method of assay given in the B. P. (1958) is a time-consuming, lengthy method unsuitable for routine continuous product control in the pharmaceutical industry. The same is true for the official method of assay given in the U. S. P. XV. There was therefore a great need for the development of a concise and time-saving method of assay for this substance.

Fritz *et al.* (3) in 1952 showed that most enols and imides can be titrated in dimethylformamide using thymol blue or azo violet indicator. Even very weakly acidic enols and imides can usually be titrated in ethylenediamine using ortho-nitroaniline indicator. Diiodohydroxyquin, which is 8-hydroxy-5,7-diiodoquinoline can be considered as enol:




* Chief Analyst, British Drug Houses (India) Ltd., Bombay, India.

As Fritz *et al.* (3) have shown, enols of the type A-$CH_2$-A′ are sufficiently acid to permit titration with sodium or potassium methoxide, provided A and A′ are groups possessing suitable electron withdrawing properties. If A and A′ are any combination of

—C—R, —C—H, —C—OR, —C—NHAr, or —C≡N, accurate titration in dimethylformamide is possible. Diiodohydroxyquin is sufficiently acid to permit titration in dimethylformamide with standard sodium or potassium methoxide solution.

## Reagents

(I) Benzene, reagent grade.

(II) Methanol, reagent grade.

(III) Dimethylformamide, technical grade.

(IV) N/10 Sodium methoxide, prepared and standardized as in U. S. P. XV. The reagent is stored in a Pyrex container protected from carbon dioxide and moisture.

(V) Thymol blue in dimethylformamide. Dissolve 1 Gm. of thymol blue in 100 ml. of dimethylformamide. A 1% W/V solution in anhydrous methanol is also satisfactory.

## Procedure

Four drops of thymol blue in dimethylformamide are added to 20 ml. of D. M. F. and the solvent is titrated with standard sodium methoxide to a clear green color to neutralize the acid impurities present. An exactly weighed amount of sample (100-200 mg. of diiodohydroxyquin) is then added to the neutralized solvent and titrated quickly with standard sodium methoxide to the appearance of green color. The color should be permanent for at least ½ minute.

Best results are obtained if titrations in dimethylformamide are carried out in vessels designed to prevent absorption of carbon dioxide from the atmosphere during the titration. The absorption of carbon dioxide may be minimized by inserting the micro-burette tip through a hole in a cork which is loosely inserted into the neck of a conical flask, the mixing being effected by means of a magnetic stirrer.

If a higher degree of precision is required, it is necessary to replace the air in the titration vessel by nitrogen.

### Calculation

1 ml. of 0.1N Sodium methoxide is equivalent to 39.697 mg. of diiodohydroxyquin

### Discussion and Results

The method given is time-saving and can be completed easily within half an hour. In accuracy, it is comparable to that of the official method in U. S. P. XV (2) as shown in Table I. The official U. S. P. XV method gives somewhat lower assay figures, when compared with above method. However, the difference between the two methods is within ± 1%.

The method can also be adopted to diiodohydroxyquin tablets. In our limited investigation, we have found that the usual tablet excipients, kaolin, and atropine salts, do not seem to interfere appreciably.

TABLE I

| *Compound* | *Sample Wt. in mg.* | *Base Normality* | *Base ml. Reqd.* | *% Purity by Nonaqueous Titration Method* | *% Purity by the U.S.P. XV Method* |
|---|---|---|---|---|---|
| Diiodohy- | 199.5 mg. | 0.0982 | 4.90 | 95.7 | 95.6 |
| droxyquin | 206.7 mg. | 0.0982 | 5.10 | 96.2 | 95.1 |
| U. S. P. | 199.1 mg. | 0.0982 | 4.90 | 95.9 | 95.5 |
| | 207.0 mg. | 0.0982 | 5.15 | 97.0 | 96.1 |
| | | | | Av. Value | Av. Value |
| | | | | 96.2 | 95.6 |

### Interfering Substances

Sulfaguanidine, phthalylsulfacetamide, and other sulfa drugs interfere. Many barbiturates, enols, and imides also interfere. Hence, diiodohydroxyquin cannot be estimated by the above method in the presence of such substances. In many cases, such interference can be eliminated by proper modifications of the method or by applying the proper correction factor.

**Summary**

(1) A rapid method for the assay of diiodohydroxyquin is presented.

(2) The method is based on the titration of diiodohydroxyquin in dimethylformamide with standard sodium methoxide solution. solution.

(3) The method can be adopted to tablets of diiodohydroxyquin; the usual tablet excipients, kaolin, and atropine salts do not seem to interfere appreciably.

(4) The method is not applicable in presence of sulfonamides, most barbiturates, and certain enols and imides.

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(2) *Pharmacopeia of the United States*, Fifteenth Revision, pp. 230-31.

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# MANAGEMENT OF LYMPHOSARCOMA THROUGH CHEMOTHERAPY

By John R. Sampey *

ONE-HALF of the patients in this study of the management of lymphosarcoma through chemotherapy were treated with nitrogen mustards. The response of 260 of the 569 patients on this therapy, however, was not given in the 93 references describing the treatments since 1949; the calculated remission rate, therefore, is 66% for this most frequently employed chemical agent in the control of lymphosarcoma.

TEM, the second most used chemical, accounts for one-fifth of the patients in Table I but a remission rate of 48%, calculated from reports giving both the number of cases treated and the number responding, leaves something to be desired. ACTH/cortisone therapy has the highest regression rate, 75%, of any of the most frequently employed chemicals in this survey.

TABLE I

CHEMOTHERAPY OF LYMPHOSARCOMA

| *Chemicals* | *No. of Cases* | *No. of Remissions* | | *No. of References* |
|---|---|---|---|---|
| | | *Good* | *Fair* | |
| N-mustards | 569 | 103 | 102 | 93 |
| TEM | 235 | 64 | 43 | 50 |
| ACTH/Cortisone | 77 | 17 | 41 | 29 |
| $P^{32}$ | 42 | 9 | 4 | 6 |
| FAA | 36 | 8 | 10 | 9 |
| Antibiotics | 27 | 1 | 11 | 12 |
| Colchicines | 26 | 2 | 5 | 10 |
| Miscellaneous | 115 | 18 | 36 | 43 |

TEM = Triethylene melamine.
FAA = Folic acid antagonists.

* Furman University, Greenville, South Carolina.

### Management With Miscellaneous Chemicals

The treatment of 115 lymphosarcoma patients with miscellaneous agents in Table I makes interesting reading for, from some of these preliminary trials, may come the drugs of large usefulness in the future control of malignant lymphomas. On the other hand, chemicals which have been employed extensively in the therapy of leukemia and Hodgkin's disease show little success in the management of lymphosarcoma.[1]

Myleran is an example of the latter type. Only Heilmeyer reported a good regression in one case of lymphosarcoma, while Hyman found no response in 3 cases. 6-Mercaptopurine has also met with large success in the chemotherapy of leukemia, but this study shows it has been tested in only 14 cases of lymphosarcoma: Bethell and Pierce each reported 2 of 3 cases had partial regressions; Farber recorded 2 of 6 patients responded to 6-MP; Rice and Sydenstricker, however, each noted no benefit in one case on 6-MP therapy.

Phosphoramides have met with more success in the control of lymphosarcoma. Wright reported one complete and 3 partial regressions in 5 patients on TEPA, and Sykes had one regression of 5 months in 2 patients on this compound, while he reported no objective improvement in 2 others on diethylenephosphoramide (DEPA). Smith observed brief benefit in 5 patients on thio-TEPA therapy.

Petrakis has recorded that 5 of 10 patients with lymphosarcoma showed objective evidence of regressions with sulfur mustards. Bernard and DeGennes each reported good regressions in one patient also, while Alpert noted improvement in both lymphosarcoma and Hodgkin's disease with sulfur mustards.

Five investigations explored the limited response of lymphosarcoma to radiogold. Chang had one patient survive 3 years on $Au^{198}$, and Hahn induced regressions by direct infiltration of the isotope into the tumors. Campbell secured no change in the volume of peritoneal fluid in one case after radiogold therapy, but Harsha found some palliation in one case. Riordan employed $Au^{198}$ in the control of lymphosarcoma, leukemia, and Hodgkin's disease.

DiPietro described 2 brief regressions in 3 patients with lymphosarcoma following ethyleneimino-quinone (E-39) therapy, and Rosa

[1] Sampey, J. R., *Am. J. Surg. 95,* 970-3 (1958); *J. So. Car. Med. Assoc. 54,* 53 (1958).

noted a fair response in one case. Hermann found the response of 2 cases disappointing, and Moulinier reported no improvement in one patient on E-39 therapy, while Verga warned that one patient's condition was aggravated by the quinone. DiPietro reported negative results in one patient on ethylenimine of picric acid.

In 2 publications, Greenspan reported brief regressions with alphapeltation. Greene and Grewe each recorded little improvement in single cases of lymphosarcoma on polydyn therapy. Ariel employed mechlorethamine oxytetracycline simultaneously on 3 patients and obtained 2 good regressions. Ollerenshaw secured a high proportion of regressions in lymphosarcoma with H-11 therapy. Opryshko noted a 4-year survival of one patient after $Co^{60}$ treatments, and this isotope with x-rays accounted for regression in one case described by Laktic.

Aragnanine induced several regressions: Wright had a 5 months' response in one of 2 cases; in 1952, Colsky reported no benefit in 3 cases but, in 1955, he noted regression of lymphadenopathy and hepatosplenomegaly in one case without any change in the hematologic status.

Bellosia employed a combination of estrogen, HN2, and x-rays to secure fair regression in one patient. Black noted some palliation with glycolic enzyme inhibitors, NaF, iodoacetic acid, malonic acid, and sodium azide. Ferradas used N-mustards, urethan, antibiotics, cortisone, and x-rays to induce palliation in 10 cases. Gellhorn described acute toxic effects in 3 cases on a pyridoxine deficient diet and treated with desoxypyridoxine. Miller noted a good response in 9 of 11 lymphosarcoma cases on a vitamin-C free diet with radiation therapy. Shanbrom described the adverse effects in 2 of 3 lymphosarcoma cases on methyltestosterone therapy.

### Limitations of Chemotherapeutic Agents

Several reports on the control of lymphosarcoma indicated that the action of the chemicals was contraindicated. Sweitzer described the death of an elderly patient on HN2 therapy due to lymphopenia, neutropenia, and thrombocytopenia. Verga reported one patient's condition was aggravated by E-39 therapy, and Arioti noted the diffusion of the neoplasm on prednisone therapy. Wintrobe lists 6-MP and FAA as showing contraindicated action in lymphosarcoma cases.

Several drugs induced marked leukopenia. Farber reported 75% of his patients showed leukopenia on 6-MP therapy, and Sawitzky described mild leukopenia on TEM therapy. DeVries found nitromin induced leukopenia in one case, and this investigator cautioned of delayed hemorrhages in CB1348 therapy of lymphosarcoma.

Ferrari has described bone damage to 6 lymphosarcoma patients treated with TEM, and Mrazek warned of similar action in both TEM and N-mustard therapy, particularly following irradiation.

## Acknowledgments

The National Library of Medicine, and the libraries of Furman University and the Greenville General Hospital made available the original literature for this study.

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# SELECTED ABSTRACTS

**The Effectiveness of Vitamin $K_1$ Derivatives in Counteracting Drug-Induced Hypoprothrombinemia.** Mushett, C. W., Kelley, K. L., and Hirschmann, R. *Blood 16:37* (1959). Menadione and its water-soluble derivatives have not been found to be effective in reversing hypoprothrombinemia induced in mammals by drugs such as Dicumarol. The authors studied the comparative effectiveness of vitamin $K_1$ emulsion and certain water-soluble derivatives of 2-methyl-3-phytyl-1,4-naphthohydroquinone-1,4-diphosphate in counteracting hypoprothrombinemia in dogs induced by Dicumarol and Dipaxin (2-diphenylacetyl-1,3-indandione). The vitamin preparations were administered intravenously, orally, and intramuscularly.

Over short periods, the 1,4-diphosphate and the 4-monophosphate water-soluble derivatives were found to be about as potent as vitamin $K_1$ emulsion when given either intravenously or orally. However, the 1-propionate-4-phosphate derivative was less potent. When given intramuscularly, the water-soluble diphosphate derivative was much more effective than the vitamin $K_1$ emulsion. The rapidity of effect was greatest following intravenous treatment with both the emulsion and the water-soluble diphosphate derivative. Intramuscular treatment gave the least rapid effect and oral therapy was intermediate between intravenous and intramuscular therapy. It was found that the emulsion was not stable in muscle tissue and that the emulsion separated into its phases following intramuscular injection.

In patients receiving prothrombin-depressing anticoagulant therapy, there are two primary indications for vitamin $K_1$ treatment; namely, inordinate hypoprothrombinemia and the need for surgery. After the prothrombin has been restored to a safe level for the required period, resumption of anticoagulant therapy is usually indicated. Therefore, careful control of the antidotal action of vitamin $K_1$ and the avoidance of a refractory state are desirable. Usually small doses of vitamin $K_1$ emulsion intravenously or orally will circumvent the development of refractoriness to the anticoagulant. However, in an emergency, such restrained therapy may be inadequate. Prophylactic and therapeutic studies reported by the authors indicated that water-soluble vitamin $K_1$ was less likely to induce refractoriness to reinstituted anticoagulant therapy than the emulsion, probably due to the shorter duration of action of the water-soluble form.

**A Long-Term Study of the Treatment of Pernicious Anemia With Folic Acid and Vitamin $B_{12}$.** Will, J. J., Mueller, J. F., Brodine, C., Kiely, C. E., Friedman, B., Hawkins, V. R., Dutra, J., and Vilter, R. W. *J. Lab. and Clin. Med. 53:22* (1959). A study of 36 patients with pernicious anemia, who were given 30 mg. of folic acid 3 times a week, was conducted over a period of up to 10 years. The effects of the administration of vitamin $B_{12}$ on selected patients from this group were investigated.

Only three of the 36 patients with pernicious anemia were maintained for the period of 10 years in a satisfactory hematologic and neurologic condition on folic acid therapy alone. The majority of these patients relapsed within the first 4 years of folic acid therapy. It was observed that those who had had no previous liver extract or vitamin $B_{12}$ therapy relapsed sooner than those previously treated with these preparations. Neurologic relapse occurred much more frequently in patients maintained on folic acid than in patients from another series from whom vitamin $B_{12}$ or liver extract was withdrawn. It was felt that folic acid may deplete the body of vitamin $B_{12}$ to the point of bone marrow exhaustion. However, the authors stated that they had found no evidence that excess folic acid increased the normal vitamin $B_{12}$ requirements of the body. Only minute amounts of vitamin $B_{12}$ were necessary to reverse the neurologic changes.

Findings from this study did not support the theory that folic acid has a direct effect on vitamin $B_{12}$ metabolism. They did suggest that minimal amounts of vitamin $B_{12}$ may become completely inadequate following the temporary stimulation of cell metabolism by excess doses of folic acid.

On the other hand, evidences found in these studies support the hypothesis that normal folic acid metabolism is dependent on an adequate supply of vitamin $B_{12}$. It would appear that vitamin $B_{12}$ influences folic acid metabolism by releasing folinic acid from its tissue conjugates, by facilitating the reduction of folic acid to folinic acid, or by promoting the formation of $N^{10}$-formyl tetrahydrofolic acid, a derivative of reduced folic acid.

The author also pointed out that these findings do not imply that vitamin $B_{12}$ functions in hematopoiesis only through folic acid metabolism.

**The Basis for Injections Containing Sufficient of a Suitable Bacteriostatic Agent.** Sykes, G. *J. Pharm. and Pharmacol. 10* Supplement: 40T (1958). The author stated that the basic requirements for a suitable bacteriostatic agent for use in injections as envisioned by the *British Pharmacopoeia* might be summarized as: (1) the ability to prevent growth of, and preferably to kill, contaminating microorganisms; (2) compatibility with the medicament; (3) low absorption rate into rubber of the closure; and (4) absence of toxicity to the patient in the quantities employed. The factors particularly considered by the author were (1) and (3).

The antibacterial properties of the bacteriostatic agents recommended by the B. P.—phenol 0.5 per cent, cresol 0.3 per cent, chlorobutanol 0.5 per cent, chlorocresol 0.1 per cent, and phenylmercuric nitrate 0.001 per cent—were studied as well as the properties of benzyl alcohol 2 per cent, dichlorobenzyl alcohol 0.1 per cent, cetrimide 0.01 per cent, methyl paraben 0.2 per cent, and propyl paraben 0.02 per cent. These agents were tested against mixed strains of *Staphylococcus aureus, Escherichia coli, Pseudomonas pyocyanea,* and mold spores. The lethal power within 24 hours of phenol, cresol, chlorbutanol, chlorocresol, phenylmercuric nitrate, benzyl alcohol, dichlorobenzyl alcohol, cetrimide, and mixed parabens was fairly good against the bacteria but only chlorocresol, phenylmercuric nitrate, and cetrimide were effective against mold spores. A reduction of one-half in the concentration of cresol, chlorobutanol, chlorocresol, and benzyl alcohol, the only agents studied at a lower concentration, was found to practically eliminate the effectiveness of the agent against bacteria and mold spores. As was to be expected, there was considerable variation from one agent to another and from one organism to another. In general, *S. aureus* was more resistant than the two gram negative organisms.

The loss of bacteriostatic agents by absorption into the rubber closures of multiple dose containers was discussed in relation to the tabulated partitioning ratios between rubber and water. The higher the distribution per cent in rubber as compared with water, the greater will be the loss of the bacteriostatic agent into rubber. Benzyl alcohol and methyl paraben had the lowest distribution in rubber with phenol, cresol, and propyl paraben reasonably low.

The author stated that the bacteriostatic agents recommended by the B. P. are probably usable but they have definite limitations,

factors which should be clearly recognized before they are considered entirely suitable in particular circumstances. He also stated that there is a need for new, more suitable bacteriostatic agents.

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**Triamcinolone Therapy in Selected Dermatoses.** Appel, B., Tye, M. J., and Leibsohn, E. *Antibiot. Med. & Clin. Ther. 5*:716 (1958). Triamcinolone (9-α-fluoro-16-α-hydroxyprednisolone) was used in the treatment of 27 patients with dermatoses in which corticosteroid therapy is definitely indicated. This new synthetic corticosteroid was used to determine its clinical effectiveness, possible undesirable side effects, and its comparative advantages over other steroids previously used. The dermatoses treated included pemphigus, systemic lupus erythematosus, disseminated neurodermatitis, and generalized dermatitis medicamentosa.

The patients in the group studied were treated over a period of a few weeks to more than a year. The initial daily dose ranged from about 8 mg. to 30 mg. in most cases. This dose was gradually reduced over the treatment period.

Excellent results, indicated by complete clearing of objective signs and marked subjective relief, were obtained in 25 cases. The other two showed good results with about 75 per cent clearing of objective signs and subjective relief. The anti-inflammatory effect of triamcinolone was found to be comparable to about one-half to two-thirds of the dose of prednisolone or prednisone.

With regard to undesirable side effects, no abnormalities of electrolytes, glucose, nonprotein nitrogen, or total protein were found and no psychiatric disturbances, complicating infections, or hypertensive changes were observed in any of the patients. One patient developed a perforated duodenal ulcer after two weeks of treatment but another patient, previously treated for gastric ulcer, showed no reactivation after one year of treatment with relatively high doses of triamcinolone.

It would thus appear that triamcinolone is an effective corticosteroid in dermatoses requiring such therapy at a lower dosage than that of previously available steroids. Side effects would also appear to be minimal.

# BOOK NOTICES AND REVIEWS

**Subsidia Pharmaceutica II.** Editors: Scientific Center of the Swiss Pharmaceutical Society (Wissenschaltliche Zentralstelle des Schweizerischen Apotheker-Vereins). 360 pp. Publishers: Swiss Pharmaceutical Society (Selbstverlag des Schweizerischen Apotheker-Vereins), Zürich, 1958. Price: 40.-Swiss Francs (approx. $10.00).

The publication of volume I of this excellent compendium (see book review, this journal, March 1958) has met with great enthusiasm and the publication of the second volume will make it even more valuable. The "Index Nominum" has been completely revised. It consists of 250 pages, listing in an alphabetical arrangement the chemical, proprietary, and non-proprietary names of drugs. One will find the structural chemical formulas, the international general titles and their corresponding titles in several pharmacopeias, the names of the manufacturers, and finally the main therapeutic action. It is the first time that this Index includes the principal therapeutic action. The information is printed on loose leaves and a separate ringbinder is provided for the "Index Nominum" in order to accommodate supplementary information at a later date. It might be stated then that the "Subsidia" consists of two parts: The Index Nominum and chapters of different contents.

The latter deal with: pharmacological action, analytical methods, new galenical preparations, small scale manufacturing equipment, tables, etc. For each of these chapters, additional sections have been written. Pharmacological action and effect of sympatholytic and synthetic antidiabetic agents are described with a listing of the more commonly used drugs. These two sections are added to the chapter on "Pharmacological Action". The chapter on "Analytical Methods" has been supplemented by a thorough discussion of the polyethylene glycols. This section presents excellent source information material with special reference to the physical and chemical characteristics of these substances. Their usefulness in the preparation of many dosage forms is described in detail.

The chapter on "New Galenical Preparations" is supplemented by an article on suppository bases. This section gives a thorough review of the literature and may serve as a well documented guide for the selection of the most desirable suppository base. For the chapter "Small Scale Manufacturing Equipment", a section dealing with filtration apparatus for injection solutions is added. A photograph of the equipment conveys the suggested procedure very simply and adequately.

Finally, tables listing the *usual* single and daily dose and also the *maximum* single and daily dose for adults are included in this volume. The route of administration is given in a special column. It is interesting to note that the Swiss Pharmacopeia and its supplements describe the maximum doses; whereas, the usual doses are based on the U. S. P., B. P., and other non-Swiss pharmacopeias.

The publication of volume II of the *Subsidia Pharmaceutica* contributes greatly to the availability of reference material which is so necessary and important for the pharmacist who must keep well informed. Even here, in the U. S. A., where many prescriptions from the countries behind the Iron Curtain are received for interpretation and for mailing, a ready reference index is of utmost importance. This reviewer will make good use of it.

ELSA EHRENSTEIN

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**Essays in Biochemistry.** Samuel Graff, Editor. x + 345 pp. John Wiley & Sons, Inc., New York 16, N. Y., 1956. Price: $6.50.

Twenty-seven authors have collaborated to honor Professor Hans Thacher Clarke on his retirement from the College of Physicians and Surgeons at Columbia University. These essays cover a wide range of biochemical subjects giving the reader a wonderful insight on some of the highly specialized thinking of these former students of Professor Clarke. The twenty-five essays deal with a variety of topics, such as: the Nature of Cancer; Lipid Metabolism; Biosynthesis of Peptide Bonds and Porphyrins; the Biochemistry of Bacterial Viruses, Ferritin, and Steroid Hormones; Glycogen Turnover, and many other phases of biochemistry.

Each of the essays contains an adequate supply of references to give the reader ample opportunity to pursue the subject further. Essentially, the chapters may be considered a brief review or critical discussion of the topic under consideration. The text is clearly written and quickly gives the reader a good grasp of the material.

This book makes for enjoyable reading on a number of currently interesting biochemical trends. Biochemists, biologists, and other workers in the medical field will find herein much of value and the book is heartily recommended to all concerned with the medical and allied sciences.

A. R. GENNARO

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**The New Chemotherapy in Mental Illness.** Edited by H. L. Gordon. xvii + 762 pp. Philosophical Library, New York 16, N. Y., 1958. Price: $12.00.

The present decade of this century will probably be remembered in medical history for the introduction of the "tranquilizing" or ataractic drugs in the treatment of mental illness. The present work, by a hundred and sixty-seven medical experts, reviews their multiple experiences with these drugs in treating such psychiatric disorders as schizophrenia, maniac depression, neuroses, mental retardation, senility, etc.

The contents are divided into four major parts: (1) generalized surveys of the drugs included in the text, (2) clinical experience with the drugs in psychiatric disease, (3) clinical experience with the drugs in related conditions, and (4) side effects of these drugs. In addition, there is a brief introduction to the subject and a comprehensive list of the drugs discussed in the book compiled according to chemical relationship.

Included in the text are methods and materials, procedures, results, discussions, and summaries of clinical observations in addition to an excellent discussion of the pharmacology and toxicology of the various ataractic agents.

Although this book does present an excellent and comprehensive review of the drugs used in mental illness, it does possess two major disadvantages: lack of an index and lack of specific references.

E. E. VOGIN

**The Relation of Psychiatry to Pharmacology.** A. Wikler. viii + 332 pp. The Williams and Wilkins Company, Baltimore 2, Md., 1957. Price: $4.00.

This book provides a comprehensive review of the literature of drugs used in psychiatry in the treatment or investigation of the "functional" behavioral disorders. It is intended not only to provide the facts which have been established by psychiatrists and pharmacologists alike, but also to present their theories, analyze their implications, and ascertain the data on which they are based.

The drugs included in this review are central nervous system stimulants, central nervous system depressants, ataractics, and agents related to the action of these drugs. The relation of these drugs to psychoses is discussed in numerous ways including their therapeutic, biochemical, neurophysiological, and psychological aspects.

One of the most important features of this book is the completeness of the bibliography, with over 850 references. An exceptionally good index rounds out this extremely useful book.

E. E. Vogin

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**Cholesterol.** David Kritchevsky. xi + 291 pp. John Wiley and Sons, Inc., New York 16, N. Y., 1958. Price: $9.75.

With the increasing volume of literature being published in very narrow phases of chemistry and other sciences, it is inevitable that someone must make an attempt to correlate as much information as possible on a particular subject. Such an effort is exemplified in this book.

The chemistry, biosynthesis, absorption and transport, and metabolism of cholesterol are discussed in the first four chapters. Cholesterol in disease states, in the blood, and the analysis of cholesterol comprise the final three chapters. The appendix lists the physical constants of cholesterol and its derivatives, serum levels, and the content of foods, human and animal tissues.

This is a comprehensive, well-documented (the literature appears to be covered through 1956) treatise of the most abundant of all steroids. Every scientific library should contain this book.

A. R. Gennaro

# American Journal of Pharmacy

The American Journal of Pharmacy is the oldest continuously published scientific periodical of its kind in America, having been established by the Philadelphia College of Pharmacy in 1825. After the original issue there were three other preliminary numbers until 1829, when regular publication began. From then until 1852 four issues were published annually, with the single exception of 1847, when an additional number appeared. Six issues a year were printed from 1853 to 1870, at which time the Journal became a monthly publication.

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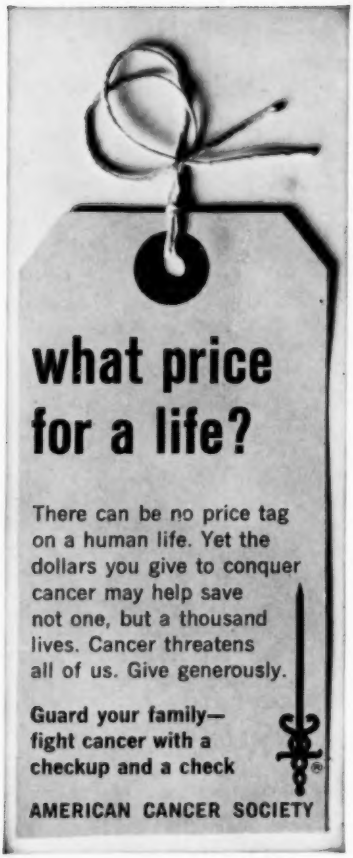
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